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TITLE: A Randomized Controlled Trial of the Group-Based Modified Story Memory Technique in TBI

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14. ABSTRACT <i>Impairments in new learning and memory (NLM) are common deficits in individuals with Traumatic Brain Injury (TBI) and exert significant negative impact on everyday life. There is thus a need for effective interventions for learning and memory dysfunction in TBI, particularly group-based interventions for which 3rd party payment may be more forthcoming. The current study addresses this need through a double blind, placebo-controlled, randomized clinical trial (RCT) of a group administration of the modified Story Memory Technique (mSMT). Over a decade of research and development at our center has demonstrated the mSMT to be effective for improving NLM in individuals with Multiple Sclerosis (MS) and TBI across three realms of functioning, objective behavior, brain functioning and everyday life. This convincing data provides Class I evidence supporting the efficacy of the mSMT for improving NLM in these populations. Given the strong efficacy data on the mSMT, coupled with the current trends in insurance reimbursement, clinicians worldwide have highlighted the need to provide the mSMT via an effective group format. We have thus modified the treatment protocol for group administration. This pilot</i>					
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1. **INTRODUCTION:**

Impairments in new learning and memory are among the most common deficits in individuals with Traumatic Brain Injury (TBI) and have been shown to exert significant negative impact on everyday life. There is thus a tremendous need for the development of effective interventions for learning and memory dysfunction in TBI, particularly group-based interventions for which 3rd party payment may be more forthcoming. The current study addresses this critical need through the conduct of a double blind, placebo-controlled, randomized clinical trial (RCT) of a group administration of the modified Story Memory Technique (mSMT). Over a decade of research and development conducted at our center has demonstrated the mSMT to be effective for improving new learning and memory in individuals with Multiple Sclerosis (MS) and TBI across three realms of functioning, objective behavior, brain functioning and everyday life. This convincing data provides Class I evidence supporting the efficacy of the mSMT for improving new learning and memory in these populations. Given the strong efficacy data on the mSMT, coupled with the current trends in insurance reimbursement, clinicians worldwide have highlighted the need to provide the mSMT via an effective group format. We have thus modified the treatment protocol for group administration. This pilot RCT tests the efficacy of a group administration of the mSMT for persons with moderate to severe TBI.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

Memory, TBI, cognition, cognitive rehabilitation, cognitive retraining, new learning, treatment

3. **ACCOMPLISHMENTS:**

What were the major goals of the project?

The current study addresses the following specific aims.

Aim 1. Objectively evaluate the efficacy of the group mSMT to improve new learning/memory in individuals with TBI with documented deficits in this area.

Aim 2. Increase the generalizability and real life application of the group mSMT by assessing outcome following group mSMT with global measures of everyday life, including one objective measure and multiple subjective measures.

Aim 3. Examine the neurofunctional changes resulting from the group-based mSMT in TBI subjects with impairments in new learning and memory. We will examine if neurofunctional changes in the brain are associated with behavioral improvements following the mSMT and if these changes are maintained over time.

Aim 4: Evaluate the long-term efficacy of the group mSMT through a 3-month follow-up.

To accomplish these aims, the following major tasks were identified:

- *Major Task 1:* Administratively Prepare for Clinical Trial
 - § *Target completion date:* 1/1/17
 - § *Actual completion date:* 1/1/17
 - § *Percent of completion:* 100%

- Major Task 2: Coordinate Study Staff for Clinical Trial
 - § Target completion date: 4/1/17
 - § Actual completion date: 4/1/17
 - § Percent of completion: 100%
- Major Task 3: Prepare Research Protocol
 - § Target completion date: 2/1/17
 - § Actual completion date: 2/1/17
 - § Percent of completion: 100%
- Major Task 4: Participant Recruitment, Treatment, Participant Evaluation
 - § Target completion date: 9/30/19
 - § Actual completion date: n/a
 - § Percent of completion: 40% (6 participants of 15 targeted)
- Major Task 5: Data Analysis
 - § Target completion date: 9/30/19
 - § Actual completion date: n/a
 - § Percent of completion: n/a

What was accomplished under these goals?

1) Major Activities:

	Deadline	Status
Major Task 1: Administratively Prepare for Clinical Trial	1/1/17	complete
Major Task 2: Coordinate Study Staff for Clinical Trials	4/1/17	complete
Major Task 3: Prepare Research Protocol	2/1/17	complete
Major Task 4: Participant Recruitment, Treatment, Participant Assessment	9/30/19	ongoing

2) Specific Objectives:

	Deadline	Status
Major Task 1: Administratively Prepare for Clinical Trial		
Subtask 1: Prepare Regulatory Documents and Research Protocol		
Finalize consent form & human subjects protocol	1/1/17	complete
Submit protocol to IRB	1/1/17	complete
Submit protocol for Military IRB Review (ORP/HRPO)	4/1/17	complete
Submit amendments, adverse events and protocol deviations as needed	As needed	
Coordinate with Sites for annual IRB report for continuing review	Annually	

<i>Milestone Achieved: Local IRB approval at KF</i>	1/1/17	complete
<i>Milestone Achieved: HRPO</i>		
Major Task 2: Coordinate Study Staff for Clinical Trials		
Subtask1: Hiring and Training of Study Staff		
Prepare job description design	11/1/16	complete
Advertise and interview for project related staff	1/1/17	complete
Coordinate for space allocation for new staff	1/1/17	complete
<i>Train staff for treatment and assessment activities</i>	3/1/17	complete
<i>Milestone Achieved: Research staff trained</i>	4/1/17	complete
Subtask 2: Facilitate hiring, training, supervision and fidelity checks as needed for attrition and treatment fidelity	ongoing	
<i>Milestone Achieved: Maintained trained and available staff throughout duration of clinical trial</i>	ongoing	
Major Task 3: Prepare Research Protocol		
Finalize administration procedures for group mSMT	2/1/17	complete
Finalize assessment procedures; assemble testing binders and testing files for NPE and AGF	2/1/17	complete
Ensure appropriate programming of ePrime stimulus delivery of neuroimaging stimuli	2/1/17	complete
Finalize timing and parameters for the collection of optimal imaging data	2/1/17	complete
Milestone Achieved: both outcome assessments and treatment protocol finalized and running smoothly	ongoing	
Major Task 4: Participant Recruitment, Treatment, Participant Evaluation		
Subtask 1: Participant recruitment & enrollment		
Begin recruitment and screening of appropriate potential participants for study participation	4/1/17	complete
<i>Milestone Achieved: 1st 3-5 participants consented, screened and enrolled</i>	5/1/17	complete
<i>Milestone Achieved: First group treatment period completed successfully</i>	7/1/17	complete
Recruitment and screening continues	ongoing	ongoing
Participants complete assigned condition group treatment to reach target n of 90	ongoing	ongoing
Complete follow-up assessments 3 months after completion of treatment	ongoing	ongoing
<i>Milestone Achieved: Data collection complete; data analysis begins</i>	9/30/19	

3) Significant results or key outcomes:

Data collection is ongoing and has been progressing well. We have recently encountered slowed enrollment and we are currently brainstorming about ways to address this. This is a very difficult study to recruit for because individuals have to come to Kessler for treatment and because it is a group treatment, their schedules need to coincide. We are currently exploring the possibility of holding the groups off-site at day treatment programs or clubhouses. There are no other results to report as data collection is ongoing.

4) other achievements.

As summarized above, this first grant year has been a very busy year. The first major task was to administratively prepare for the study. This included preparing regulatory documents and the research protocol, which consisted of multiple time-consuming processes including preparing consent forms and human subjects protocols, local IRB review, military IRB review, etc. This was all achieved on time. The second major task was to coordinate the study staff for the clinical trial. This is also a time-consuming processing that involves hiring the appropriate staff, training all staff on assessment and treatment procedures, ensuring the adequacy of training, advertising for the study, compiling all assessment and training protocols, coordinating space allocation, and identifying technological needs and capabilities. This was also all completed on time. Major Task 3 required the preparation of the research protocol including the treatment administration procedures, both neuropsychological and neuroimaging assessment procedures, and timing, all of which was completed on time. Finally, we were able to initiate participant recruitment, testing and enrollment. The first group completed treatment successfully and we are ready to begin the 2nd group now. Recruitment has been increasingly difficult, detailed below. We are thus exploring additional options for recruitment.

Recruitment details:

- **249** people with moderate to severe TBI were contacted for potential participation in the study.
 - **33 of the 249** were background screened
 - § 18 didn't qualify based on background screen.
 - § 15 people qualified based on the background screen
 - 8 people were brought in for in-person screen.
 - 1 person failed the in-person screen
 - 1 person qualified based on the in-person screen, but decided not to participate due to the time commitment.
 - 6 people are enrolled, 4 of which completed the study.
 - § 3 of these people were contacted multiple times to schedule in-person screen, but never got back.
 - § 1 person was scheduled for in-person screen, cancelled appointment and isn't free to participate until 2018.
 - § 3 other people are not free to participate until 2018.
 - **57 of the 249** were not interested due to time commitment or couldn't travel to us
 - **130 of the 249** could not be reached after multiple attempts and did not return our calls
 - **2 of the 249** moved out of state
 - **3 of the 249** asked to be called back in a few weeks or months
 - **24 of the 249** did not qualify based on information garnered during a casual conversation (e.g. had a stroke rather than TBI)

What opportunities for training and professional development has the project provided?

This project was not intended to provide training and professional development. However, staff recruited for the study include bachelor's level research assistants that received substantial on-the-job training in neuropsychological assessment, working with persons with

TBI and the cognitive rehabilitation protocol being studied. This is done through one-on-one work with a mentor and results in increased knowledge or skill in neuropsychological assessment and functioning. All study staff additionally participate in the semi-annual TBI Consumer Conference held (9/29/2017 this year) and have many opportunities to attend lectures and workshops at Kessler or Rutgers University.

How were the results disseminated to communities of interest?

Nothing to Report. Data collection is ongoing.

What do you plan to do during the next reporting period to accomplish the goals?

Goals for the next reporting period focus on participant recruitment, enrollment and treatment. We will be meeting with local day treatment TBI programs to explore holding the groups at their center. This will ease the burden of participation for the participants and hopefully facilitate increased recruitment. This is a bit challenging due to technology needs, but it should be possible. We will be continuing to run groups at Kessler Foundation as well and we will be working with our newly hired patient recruitment specialist to increase awareness of the study in the TBI Community and hopefully referrals for participation. We hope this 2-pronged approach to recruitment, both new approaches, serve to increase our rate of enrollment.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report. Data collection is ongoing.

What was the impact on other disciplines?

Nothing to Report. Data collection is ongoing.

What was the impact on technology transfer?

Nothing to Report. Data collection is ongoing.

What was the impact on society beyond science and technology?

Nothing to Report. Data collection is ongoing.

5. CHANGES/PROBLEMS:

While we are exploring different options for recruiting participants, this will not involve any changes to the study protocol. All methodology will remain as proposed.

Changes in approach and reasons for change

none

Actual or anticipated problems or delays and actions or plans to resolve them

The only anticipated delay is the delay in recruitment that we have already encountered and is already being addressed

Changes that had a significant impact on expenditures

none

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

none

Significant changes in use or care of human subjects

none

Significant changes in use or care of vertebrate animals.

none

Significant changes in use of biohazards and/or select agents

none

6. PRODUCTS:

Nothing to Report. Data collection is ongoing.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Nancy Chiaravalloti, PhD; PI; no change

Glenn Wylie, D.Phil.; co-I; no change

John DeLuca, PhD; co-I; no change

Nancy Moore, MA; Research Manager; no change

Name:	<i>Ekaterina Dobryakova, PhD</i>
Project Role:	<i>Co-investigator (replaced Helen Genova, PhD)</i>
Nearest person month worked:	<i>5</i>
Contribution to Project:	<i>Dr. Dobryakova provides imaging expertise in the day to day data</i>

	<i>collection of the functional imaging data</i>
Funding Support:	<i>National MS Society</i>

Name:	<i>Tiffany Chang</i>
Project Role:	<i>Research Assistant</i>
Nearest person month worked:	<i>5</i>
Contribution to Project:	<i>Ms. Chang has been involved with participant recruitment and conducting the baseline and follow-up assessments</i>
Funding Support:	<i>National MS Society</i>

Name:	<i>Donya Green</i>
Project Role:	<i>Research Assistant</i>
Nearest person month worked:	<i>4</i>
Contribution to Project:	<i>Mr. Green has been involved with participant recruitment and conducting the treatment sessions</i>
Funding Support:	<i>NIDILRR Field Initiated grant</i>

Name:	<i>Eric Stone</i>
Project Role:	<i>Research Assistant</i>
Nearest person month worked:	<i>1</i>
Contribution to Project:	<i>Mr. Stone has been involved with participant recruitment.</i>
Funding Support:	<i>National MS Society and NJ Commission on TBI Research</i>

Name:	<i>Michael Pellicane</i>
Project Role:	<i>Research Assistant</i>

Nearest person month worked:	2
Contribution to Project:	<i>Mr. Pellicane had been involved with participant recruitment and conducting the treatment sessions. He has now left the organization.</i>
Funding Support:	<i>NIDILIRR Field Initiated grant</i>

Has there been a change in the active other support of the PD/PI (s) or senior/key personnel since the last reporting period?

Nothing to Report.

What other organizations were involved as partners?

None. Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

none

9. APPENDICES:

none